REMARKS

The rejection of Claims 1-13 under 35 U.S.C. § 102(b) as anticipated by U.S. 4,686,243 (Keil et al) is respectfully traversed.

The present invention relates to a method for the preparation of crosslinked enzyme aggregates (CLEAs), crosslinking agents used in said method, and other methods of using the crosslinking agents.

As described in the specification in Background of the Invention, beginning at paragraph [0002], CLEAs can be regarded as self-supported immobilized enzymes, and which have been used in many fields. In the art, CLEAs are prepared by precipitating the enzymes of interest by a precipitating agent for aggregating the enzymes, which are then crosslinked to one another by a crosslinking agent such as glutaraldehyde.

The present invention is deemed to be an improvement over the above-discussed prior art. As recited in above-amended Claim 1, the invention is a method for the preparation of crosslinked enzyme aggregates, comprising the steps of: A – providing a plurality of enzyme molecules, B – aggregating the enzymes in a liquid medium, comprising a precipitating agent, C – crosslinking the aggregated enzymes to one another by providing a crosslinking agent in the liquid medium, wherein the crosslinking agent is prepared by combining a first and a second compound each having at least two reactive groups, the reactive groups of the first compound being primary amino groups, the reactive groups of the second compound being aldehyde groups.

Keil et al is drawn to a crosslinked, porous, bead-like copolymer useful as a support for the fixation of enzymes, which copolymer is composed of five different monomer groups. Keil et al further disclose that to immobilize enzymes, the copolymer is advantageously activated using a diamine and a dialdehyde, preferably glutaraldehyde. The supports are loaded using an aqueous enzyme solution which can contain a buffer, and are incubated in the

enzyme solution at room temperature for a certain period of time, after which the aqueous solution is separated off, whereby the copolymer can be employed as a biocatalyst (column 8, lines 3-18). Example 10 exemplified activation of the copolymer support, first with the diamine, after which the support is washed until free of amine, and then activated with the glutaraldehyde, after which a lipase is fixed to the activated support. Example 11 is similar, but uses a different diamine.

Keil et al neither disclose nor suggest the presently-claimed invention. First of all, Keil et al is not concerned with a method of making CLEAs. Rather, Keil et al is concerned with making and activating a particular copolymer support, which support is then used for fixing or immobilizing an enzyme. While the present invention may use a particular amine and a particular aldehyde, which may overlap with those of Keil et al, this is merely coincidental, because Keil et al use their diamines and dialdehyde for a different purpose. Nor does Keil et al disclose or suggest the presently-claimed crosslinking agent. In Keil et al, as described in Example 10 therein, the diamine is removed before the dialdehyde is applied. Thus, Keil et al teach away from the combination of diamine and dialdehyde.

For all the above reasons, it is respectfully requested that the rejection over Keil et al be withdrawn.

The rejection of Claims 7 and 10-13 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Indeed, the rejection is now moot in view of the above-discussed amendment. Accordingly, it is respectfully requested that it be withdrawn.

The objection to Claims 10-13 is respectfully traversed. The Examiner only refers to Claim 13, which claim has been cancelled. Note that whether a claim begins with an article, such as "a" or "the", is simply a matter of style, and does not effect the meaning of the claim. Accordingly, it is respectfully requested that the objection be withdrawn.

Applicants note that the copy of the Form PTO-1449 from the Information Disclosure Statement (IDS) filed February 28, 2002, does not contain the Examiner's initials in the appropriate box. Accordingly, **submitted herewith** is another copy of this Form PTO-1449. The Examiner is respectfully requested to properly initial the form, and include a copy thereof with the next Office communication.

Finally, also **submitted herewith** is a Replacement Sheet for the drawing containing Figs. 1 and 2. Spermidine is an asymmetric molecule H_2N-$(CH_2)_3$-NH-$(CH_2)_4$-NH_2, and the formula thereof has been corrected accordingly in Fig. 2. The formulae for the "monomer" and "polymer" in Fig. 2 have also been corrected accordingly. The additional descriptive matter added at the bottom of Fig. 2 signifies that due to the asymmetry of spermidine, several polymers can be formed, such as head to head, head to tail, tail to tail, etc. In addition, parts A-D of Fig. 1 have been relabeled as Fig. 1A, Fig. 1B, etc.

All of the presently-pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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